

Cardiovascular, pharmacology and chemistry

Committee:

Dr. Wilson, Chm.
Dr. Jacobson
Dr. Cattell

#346

TOBACCO INDUSTRY RESEARCH COMMITTEE
150 East Forty Second Street, New York 17, N. Y.

Application for Research Grant

Date: April 10, 1962

1. Name of Investigator: Anthony A. Albanese, Ph.D.
2. Title: Director, Nutrition and Metabolic Research Division.
3. Institution and Address:

The Winifred Masterson Burke Relief Foundation
The Burke Foundation Rehabilitation Center
White Plains, New York.

4. Project or Subject: The Effect of Nicotine on Protein and Amino Acid Metabolism in Humans.
5. Detailed Plan of Procedure:

It has long been known that when smokers stop smoking there usually occurs a gain in body weight. The report of Professor R. D. Passey on his studies with rats exposed to cigarette smoke shows that cessation of smoke exposure is associated with a return to normal urea nitrogen excretion.

The foregoing observations suggest that it would be fruitful to study in detail the effect of smoking on the nitrogen metabolism of humans. The experience of the Principal Investigator and his associates indicates that changes in the amino acid levels of the blood provide an accurate criterion of protein utilization.¹ To this end, chromatographic methods have been developed which permit

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analysis of amino acid content of blood with samples of 0.1 or 0.2 ml. which are obtained by fingerprick. These procedures have made possible the rapid screening of the effects of various agents (hormones, enzymes, and other substances) on protein and amino acid metabolism.^{2, 3, 4, 5}

In applying this experience to the present problem, it is planned to determine the blood amino acid pattern of heavy smokers and non-smokers. Smokers will be asked then to stop for one or two weeks, and determinations of blood amino acid levels will be made during the period of abstention. The interval of abstention may be prolonged or shortened, depending on the findings. In these studies, each subject will serve as his own control which will avoid some of the problems arising from genetic heterogeneity.

In addition to the aforementioned measurements, it is planned to determine also the effects of smoking in terms of the utilization of protein load tests as determined by post-absorptive changes in blood amino acid levels. Professor Passey's report suggests that the pattern of utilization of the load tests may differ between smokers and non-smokers. On the basis of available knowledge, it is expected that the effects of smoking should exhibit themselves primarily with changes in the utilization of the aromatic amino acids.

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It is estimated that the studies outlined will require a year for their completion. If our findings prove promising, it is proposed to extend the investigations with measurements of nitrogen balance in addition to the determination of blood amino acid levels. It is felt that it is of considerable importance to demonstrate the magnitude of the effect of smoking on the storage of nitrogen. Although the amino acid levels provide a good measure of this effect, the need for nitrogen balance data is considered to be acute, since this is generally associated with changes in body weight.

References:

1. Albanese, A. A.: Criteria of Protein Nutrition, in "Protein and Amino Acid Nutrition." (Albanese, Ed) Academic Press, New York, 1959.
2. Albanese, A. A., Lorenze, E. J., and Orto, L. A.: Nutritional and Metabolic Effects of Some Newer Corticosteroids. N. Y. State J. Med. 61: 3998-4002 (1961).
3. Albanese, A. A., Lorenze, E. J., and Orto, L. A.: Nutritional and Metabolic Effects of Some Newer Steroids. I. Oxandrolone and Triamcinolone. N. Y. State J. Med. (1962). In Press.
4. Albanese, A. A.: General Nutrition of the Aging Patient with Some Observations on Specific Metabolic Needs, presented as part of a Colloquium on "The Pharmacological Principles of the Aging Patient," Clinical Section of the Gerontological Society, Nov. 10, 1961, Pittsburgh, Penna. Joseph T. Freeman, M. D., Chairman. Also: in "Principles of Drugs in the Elderly," Charles C Thomas Co In Press.

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5. Albanese, A. A., Otto, L. A., Thompson, G. F., and Eisenberg, A. Individuality of Protein and Amino Acid Needs. Federation Proc. 21: 403 (1962).

6. Budget Plan:

Salaries:

Supervisory personnel
Research technician
Test subject fees
Overhead - 10%

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Total

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7. Anticipated duration of work: Two years.

8. Facilities and Staff Available:

The Burke Foundation Rehabilitation Center, registered by the American Medical Association, offers coordinated services based on the philosophy of helping the individual attain maximum physical, psychological, social, and economic functioning.

The laboratory occupies the entire first floor of one of the annex buildings which comprises an area of approximately 3600 square feet, divided into thirteen rooms. It is equipped with the latest apparatus and devices necessary for our type of work. These include: a complete micro Kjeldahl unit, two analytical balances, six centrifuges, six thermostatically controlled ovens, three photoelectric colorimeters, one recording densitometer, two ultrabaths, two 2-pan baths, one recording spectrophotometer, one flame photometer, one Aminco portable electrophoresis apparatus, one metabolator. In addition, we have a number of home-built units, such as chromatogram

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cabinets and paper electrophoresis apparatus. Ample supplies of expendables, such as glassware and chemicals, are on hand.

The personnel of the Division is comprised of the Director (Principal Investigator) and his Assistant, an Administrative Assistant, two full-time Research Assistants, and four part-time Research Technologists who are assigned full-time to the Research Program of the Division. Temporary personnel include college students in training for Laboratory Technologists.

9. Additional Requirements:

During the second year of the study, when it is planned to do nitrogen balance as well as blood amino acid level determinations, it is expected that the cost of the researches will be increased due to the additional laboratory time, as well as additional test subjects required. It is estimated that these items will amount to approximately \$3,500., making a total cost for the second year of the study approximately \$11,000.

10. Additional Information:

The basic body of experience and information relative to the tests and test procedures to be employed in this investigation have been obtained in long-term projects supported by the Office of Naval Research, Air Force, and Sugar Research Foundation. Pertinent publications follow:

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(From Annotated Bibliography of A. A. Albanese)

#121. Metabolic Significance of Blood Amino Nitrogen Levels. A. A. Albanese, L. A. Orto, and D. N. Zavattaro. Federation Proc. 15, 210 (1956). Averages of fasting blood amino N levels of 22 children (5 - 15 yrs.) and 101 adults (40 - 95 yrs.) showed good statistical correlation with the degree of malnutrition expressed in percentage of underweightness. It was found that blood amino N increments 1 hour following oral protein dosages (adults, 0.2 gm/Kg, and children, 0.4 gm/Kg) provided a more accurate criterion of protein nutritional status than fasting amino N levels alone.

#137. Biochemical Significance of Plasma Amino Nitrogen in Man with a Comparison of Other Criteria of Protein Nutrition. A. A. Albanese, L. A. Orto, and D. N. Zavattaro. Metabolism 7, 256-265 (1958). A comparison of the correlation of fasting plasma amino nitrogen levels, plasma amino nitrogen increments with a protein load, blood protein levels and nitrogen balance, with deviations from desirable body weight have been made on some 200 adults. The findings suggest that measurements of plasma amino nitrogen may provide a useful criterion of protein nutrition.

#139. Proteolytic Enzyme Supplements and Protein Utilization in Man. A. A. Albanese, R. A. Higgins, L. A. Orto, and D. N. Zavattaro. Federation Proc. 17, 179 (1958). Studies were undertaken to determine the effect of digestive enzyme administration on the absorption rate of milk proteins in terms of plasma amino nitrogen change. The 13 healthy normal children studied showed no significant change in plasma amino nitrogen index with enzyme administration. Results in 60 adults disclosed that enzyme administration significantly increased the plasma amino nitrogen index of 19 subjects. These increases were most frequently associated with malnutrition and advanced age. Aminograms revealed that positive responses generally included significant increases in essential amino acid content of the blood, especially methionine, threonine and lysine. Chromatographic analyses of in vitro enzyme-milk protein digests indicated that the amino acid pattern changes of the blood in the oral tests could be ascribed to the enzyme supplement.

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#143. Plasma Amino Nitrogen Levels and Protein Needs of Young Children. A. A. Albanese, R. A. Higgins, and L. A. Orto. Federation Proc. 18, 179 (1959). Serial measurements were done for periods of 1 to 25 weeks on 14 infants (2 to 24 months) who had suffered varying degrees of nutritional depletion incident to disease or surgical processes. Results show that decrements in rate of body weight change are accompanied and often forecast by significant decreases in resting plasma amino nitrogen levels. Conversely, increments in rate of body weight change are frequently associated with increasing resting plasma amino nitrogen. Decrements in plasma amino nitrogen and/or body weight followed protein intakes of less than 5.0 gm/kg/day. Adequacy of this level of food intake varied directly with the protein source and prevailing metabolic state of the subjects.

#145. Nutritional Significance of Plasma Amino Acid Levels. A. A. Albanese and L. A. Orto. Scientific Exhibit. Ann. Meeting Fed. Am. Soc. Exper. Biol., Atlantic City, N. J., June, 1959. Copyright 1959. The availability of amino acids was determined from differences in blood levels immediately before and one hour after test meals which supplied proteins and calories in amounts usually consumed by infants and young children. Test feedings with a low protein infant formula (1.7 gm.%) were associated with a decrease in plasma lysine as well as total plasma amino nitrogen. Conversely, feedings with conventional whole or evaporated milk formulas were associated with increases in plasma lysine and total plasma amino nitrogen. Ingestion of milk or egg proteins (0.25 - 0.50 gm/kg) causes an increase in the lysine content of the blood of young children. Ingestion of cereal or white bread proteins causes a decrease in the lysine concentration of the blood of young children. Supplementation with lysine provides a physiological technique for overcoming the plasma lysine lowering effect of the foods tested. (Copies enclosed)

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Biographical Sketch:

Albanese, Anthony August, Principal Investigator

Born:

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Education:

B.S. - New York University 1930
Graduate Work - University of Budapest 1930-32
Ph. D. - Columbia University 1940

Assignments:

Research Assistant - Dept. Pathology, Coll. of P & S, Columbia
Univ. 1933-40

Research Associate - Div. of Chem., NIH, 1940-41

Associate in Pediatrics and Research, Johns Hopkins Univ.
1941-45

Assistant Professor of Pediatric Biochemistry, N. Y. Univ.
Coll. of Med. 1945-48.

Associate Professor of Pediatric Biochemistry, N. Y. Univ.
Coll. of Med. 1948-49

Director of Research, St. Luke's Conv. Hospital, 1949-50

Director of Nutrition and Metabolic Research Division, The
Burke Foundation 1959--

Director of Geriatric Nutrition Laboratory, Miriam Osborn
Memorial Home 1959--

Honorary Positions:

American-Hungarian Exchange Fellow 1930-32

Fellow - Hungarian Ministry of Education, Summers 1931 and 1932

Corn Industries Fellowship 1940-41

Responsible Investigator for Office Scientific Research &
Development U.S. Gov't. Committee on Med.
Research 1941-45

Responsible Investigator for Office of Naval Research 1945--

Responsible Investigator for Air Research and Dev. Command 1960--

Associate Editor, N. Y. State Journal of Medicine 1959--

Special Societies:

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Publications:

164 publications in the field of human nutritional research and
methods are contained in 5 books

Certifications:

Specialist in Human Nutrition, Am. Board of Nutrition

Diplomata Mexican Gerontological Society and Mexican
Society of Geriatrics 1956 (Honorary)

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Signature Anthony A. Albanese
Director of Project

George Bush
Business Officer of the Institution

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